Xgeva™ (denosumab injection for subcutaneous use)

Effective Date: 10.25.11
Date Developed: 10.07.11 by A. Reeves MD
Last Approval Date: 01.26.16, 01.24.17

Xgeva is a monoclonal antibody with affinity for nuclear factor-kappa ligand (RANKL). Osteoblasts secrete RANKL; RANKL activates osteoclast precursors and subsequent osteolysis which promotes release of bone-derived growth factors, such as insulin-like growth factor-1 (IGF1) and transforming growth factor-beta (TGF-beta), and increases serum calcium levels. Denosumab binds to RANKL, blocks the interaction between RANKL and RANK (a receptor located on osteoclast surfaces), and prevents osteoclast formation, leading to decreased bone resorption and increased bone mass in osteoporosis. In solid tumors with bony metases, RANKL inhibition decreases osteoclastic activity leading to decreased skeletal related events and tumor-induced bone destruction. In giant cell tumors of the bone (which express RANK and RANKL), denosumab inhibits tumor growth by preventing RANKL from activating its receptor (RANK) on the osteoclast surface, osteoclast precursors, and osteoclast-like giant cells.

Pre-Authorization Criteria:

Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy; Prevention of skeletal-related events (e.g. fracture, spinal cord compression, bone pain requiring surgery/radiation therapy) in patients with bone metastases from solid tumors; treatment of giant cell tumor of the bone in adults and skeletally mature adolescents that is unresectable or where surgical resection is likely to result in severe morbidity.

Note: Xgeva is not indicated for prevention of skeletal-related events in patients with multiple myeloma. Bone destruction caused by RA is an off label use and therefore not covered. Please refer to the VCHCP policy on Prescription Medications for Off Label Use for more details.

VCHCP requires that Xgeva by prescribed by an oncologist.

Dosing/Administration: The recommended dose is 120 mg subcutaneously (SC) given every 4 weeks in the upper arm, upper thigh, or abdomen. Give calcium and vitamin D as needed to treat or prevent hypocalcemia.

Safety/Tolerability:
Contraindications: None.¹

Warnings/Precautions: Hypocalcemia; Osteonecrosis of the jaw; Pregnancy Category: C.

Adverse Events (AEs): The most commonly observed AEs in those receiving Xgeva (per-patient...
incidence greater than or equal to 25%) were fatigue/asthenia, hypophosphatemia, and nausea. Dyspnea was the most common serious adverse reaction in patients. Osteonecrosis and hypocalcemia were the most common adverse reactions that led to Xgeva discontinuation.

References:
26. ©2015 UpToDate® www.uptodate.com
**Revision History:**

Date Reviewed/ No Updates: 04.02.12; 01.16.13 by A. Reeves, MD  
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<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Content Revised (Yes/No)</th>
<th>Contributors</th>
<th>Review/Revision Notes</th>
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</thead>
<tbody>
<tr>
<td>1/24/17</td>
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<td>Catherine Sanders, MD; Robert Sterling, MD</td>
<td>Annual review</td>
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</tbody>
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